R-035

Interruptions in Gene Expression Drive Operons to the Leading Strand of DNA Replication

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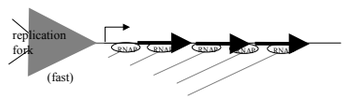
Abstract

Which genes are strongly biased to the leading strand?
- Essential genes
- Operons
  - Stronger bias for highly expressed or ubiquitous operons

Why are genes selected to the leading strand?
- Genes on the leading strand experience head-on collisions between DNA and RNA polymerases
- Head-on collisions slow the fork
  - Slowing the fork doesn't explain why essential genes show the strongest bias
- Head-on collisions interrupt gene expression for longer
  Explains the strand bias of essential genes & operons

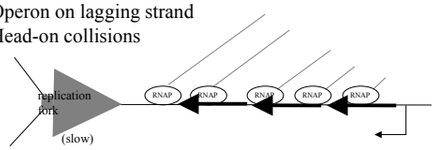
The Difference Between Strands

Operon on leading strand
Co-directional collisions



Interruptions:
1 s. for 1st gene
3 s. for 3rd gene

Operon on lagging strand
Head-on collisions



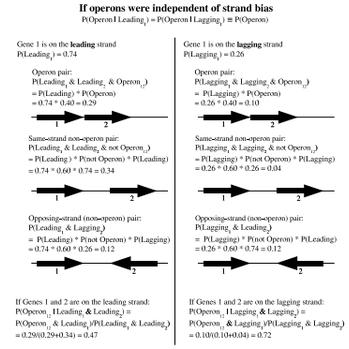
Interruptions:
5 s. for 1st gene
15 s. for 3rd gene

If Operons Were Independent of Bias

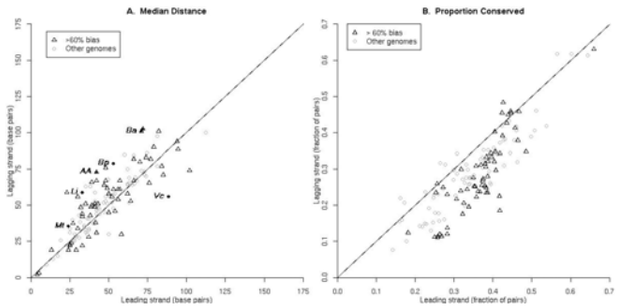
Operon pairs are
- closer together
- more conserved

Lagging-strand pairs are unlikely to arise unless they are operons (see right)

Lagging-strand pairs would be
- closer together
- more conserved



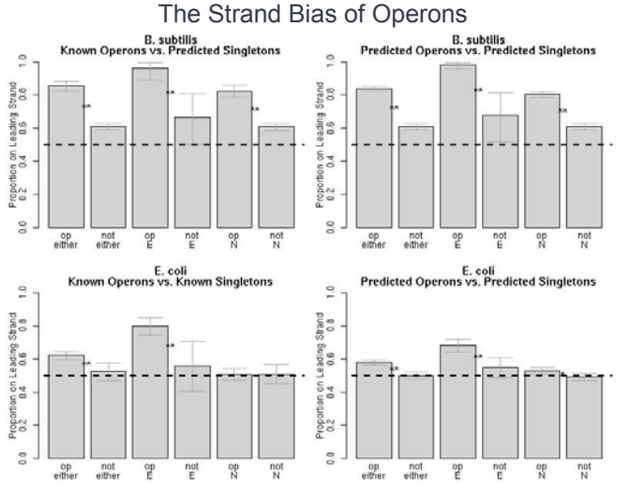
Operons Are Biased to the Leading Strand in Most Bacteria



Theories of Strand Bias

- Lagging strand slows the replication fork (Brewer)
  - Inconsistent with strong bias of essential genes relative to other highly expressed genes (Rocha)
- Toxic truncated peptide hypothesis (Rocha)
  - Does not explain bias of operons
  - Inconsistent with the peptide tag of tmRNA being non-essential
- Collisions (briefly) interrupt gene expression
  - Leading strand slows the fork => longer interruptions
  - Interrupting expression of essential genes or ubiquitous operons is more deleterious
  - Interruptions are longer for genes in operons
  - Interruptions are longer for highly expressed genes?
- Weak selective force => weak effect
  - Not observable for every chromosome or every type of gene

The Strand Bias of Operons



Stronger Bias for Highly Expressed and Ubiquitous Operons